



REMARKS

Claim 59 has been amended for clarity. Claims 1-11, 26-29, 32, 33 and 58-65 are currently under examination.

Objections to the Drawings

The proposed drawing correction of Figure 1 has been approved. A transmittal of formal drawings is being filed herewith.

Rejection Under 35 U.S.C. §112, 2d Paragraph

Claim 59 is rejected as indefinite for lacking antecedent basis for the term "subset of NMDA receptors." This rejection has been met by amending claim 59 to recite "a plurality of NMDA receptors," a term that can be found in the base claim. Accordingly, the rejection should be withdrawn.

Rejection Under 35 U.S.C. §103

Claims 1-19, 11, 26-29, 32, 33 and 58-65 are rejected as unpatentable over Park-Chung in view of Williams, Daggett, Masuko and Traynelis, all previously cited by the Examiner in the first office action. The Examiner maintains that the motivation to modify Park-Chung to include elements found in the other, secondary references can be found in:

the recognition that determination of the effect of the drug substances on specific receptor subunits or mutations should permit development and screening receptor subtype-specific or disease-specific drugs and reduction of unwanted side effects, as suggested by Daggett et al. (...column 15, 4th and 5th paragraphs) and the expression of recombinant NMDA receptors in, e.g., *Xenopus oocytes*, provides an ideal approach to examine the biological functions of the NMDA receptors and to evaluate the effect of modulators on the NMDA receptors, as demonstrated by [all 5 cited references]. (Office Action, page 6).

This rejection is respectfully traversed. To establish prima facie obviousness of a claimed invention, the prior art must provide (a) a motivation to combine or modify the reference(s) to arrive at the claimed invention, and (b) a reasonable expectation of success. The mere fact that references (in this case, five references) can be combined does not render the

resultant combination obvious unless the prior art also suggests the desirability of the specific combination as claimed. See MPEP § 2143.01. The Federal Circuit has made it clear that "it is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious." *In re Fritch*, 972 F.2d 1260 (Fed. Cir. 1992). In this case, the Examiner has used impermissible hindsight to pick and choose different elements of as many as five different pieces of prior art to come up with the claimed methods, and the Examiner has done so in the absence of a suggestion in these references to combine the references to arrive at the specifically claimed methods. The required motivation to combine must be a specific motivation. For example, for claim 1, there must be a specific motivation to, *inter alia*, screen steroid-based molecules as modulators of NMDA receptor by an assay that includes providing a plurality of recombinant NMDA receptors which differ in their subunit identity, and requires the use of a neurotransmitter recognition site ligand. This motivation is clearly not found in the cited references; much less so for the specific methods of the narrower dependent claims.

The Examiner relies on a passage in Daggett that discusses screening assays in general to infer a motivation to arrive at the present claims. However, the passage in Daggett relied on by the Examiner is so broad as to be meaningless. It offers no more than a general suggestion or invitation to experiment. Furthermore, there is no suggestion in Daggett that the passage relied on by the Examiner refers to anything more than possible uses for the specific receptor subunits that are described and claimed in the Daggett patent. Thus, Daggett neither provides a specific motivation to arrive at the elements of claim 1 in combination, nor provides a reasonable expectation of success. The Examiner's merely conclusory statements that the five references combined "demonstrate" the elements of the claims is, of course, not sufficient to provide the required motivation or expectation of success. Accordingly, a prima face case of obviousness has not been made and Applicants respectfully request that the rejection be withdrawn.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant : Farb et al.
Serial No. : 09/652,345
Filed : August 31, 2000
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Attorney's Docket No.: 13594-010002

Applicant asks that all claims be allowed. Enclosed is a Petition for Extension of Time
with the required fee. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 12 November 2002



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